Genomic Factors and Population Health

Most human disease results from interaction between inherited genetic variations and environmental factors like diet, infections, lifestyle, chemicals, and social conditions. The discovery of thousands of variants will doubtless increase our understanding of the role of genetic variation in disease, death, and disability. One benefit of this ongoing research may be an increase in the understanding of disease occurrence in populations, which could provide new opportunities for prevention and intervention.

Three major efforts to make these genomic discoveries usable for improving population health are under way:

- Integrating genomics into Acute Public Health Investigations (APHIs),
- Analyzing genetic variations in the National Health and Nutrition Examination Survey (NHANES) III DNA Bank, and
- Expanding the Human Genome Epidemiology Network (HuGENet™).

Acute Public Health Investigations

An Acute Public Health Investigation is a timely assessment of adverse health events followed by rapid application of prevention and control measures that are already available. Conducting APHIs that employ epidemiologic and laboratory methods has long been recognized as a key responsibility of the nation's public health system.

Increased knowledge of the role of human genomics in disease causation sharpens response to acute public health events. It may be useful to consider human genomics in investigations of the following:

- Disease clusters (e.g., infectious disease outbreaks, clusters of cancer or birth defects),
- Exposure clusters (e.g., environmental, occupational, bioterrorism), and
- Adverse reactions to therapeutics (e.g., vaccines, antibiotic prophylaxis, blood products).

Research that could lead to enhanced prevention, detection, and control of future adverse health events includes assessment in the following areas:

- Genomic profiles (e.g., relation to susceptibility, resistance, severity, prognosis, interactions with other risk factors, and response to therapeutics),
- Exposure profiles (e.g., use of mRNA transcripts to estimate exposure levels or characterize exposure), and
- Outcome variation (e.g., use of protein expression to characterize outcomes).

This information may aid in identifying causes of adverse health events and directing public health and clinical interventions, such as vaccination, exposure reduction, behavioral intervention, and therapeutics. CDC, in collaboration with the Council of State and Territorial Epidemiologists, formed a multidisciplinary APHI Working Group to assess needs, develop tools, and establish priorities for studying human genomic factors in the context of APHIs. In May 2004, the APHI Working Group, which includes external consultants who provide additional expertise and guidance, conducted a workshop in order to develop a research agenda to integrate human genomics into APHIs.

NHANES III DNA Bank

The National Health and Nutrition Examination Survey (NHANES) is a nationally representative survey of the U.S. population conducted by CDC's National Center for Health Statistics (NCHS). During the second phase of NHANES III (1991–1994), white blood cells were frozen and cell lines were immortalized to create a DNA bank.

A CDC-wide working group of epidemiologists and laboratory scientists developed a collaborative proposal for determining the prevalence of selected genotypes of public health importance using the NHANES III DNA Bank. The criteria used to select genes for the proposal included the following:

- Known or hypothesized association with diseases of public health importance,
- Role in pathways affecting multiple diseases,
- Identified functional variants,
- Relatively common variants (prevalence >2.0%),
- Previously described gene–environment or gene–gene interactions,
- Relevant phenotypic data available in NHANES data sets, and
- No current use for clinical risk assessment or intervention.

The final approved proposal included 87 variants of 57 genes known to be important in at least six major pathways: nutrient metabolism; immune and inflammatory responses; activation and detoxification pathways; DNA repair pathways; hemostasis and renin/angiotension pathways; and developmental pathways.

Genotyping will be performed in collaboration with the National Cancer Institute (NCI) at the NCI Core Genotyping Facility. A steering committee composed of CDC's Office of Genomics and Disease Prevention (OGDP), NCHS, and NCI representatives will provide oversight for the laboratory and analytic aspects of the study. An additional proposal to analyze the genotype–phenotype data from NHANES is in development by the NCI/CDC collaborative group.

Data from the NHANES database will provide a basis for future analysis of gene–disease associations and gene–environment interactions. Establishing the prevalence of gene variants known to interact with specific environmental factors will provide a foundation for developing and assessing the potential impact of environmental interventions.

HuGENet™

The Human Genome Epidemiology Network (HuGENet™) is a global collaboration of individuals and organizations committed to assessing the role of human genome variation in population health and the potential of genomics for improving health and preventing disease. Through collaborative research, systematic reviews, training, and information dissemination, HuGENet™ seeks to advance our global knowledge based on population prevalence of human genetic variation, association between genetic variants and human diseases, measurement of gene–environment interaction, and evaluation of genetic tests for screening and prevention. This knowledge is fundamental to the evidence-based integration of human genomics into the practice of medicine and public health in the 21st century.

For more information, please visit CDC's Office of Genomics and Disease Prevention Web site at http://www.cdc.gov/genomics.